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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/798,876	03/11/2004	Arthur E. Uber III	IN/02-002.PCT/US.C	4883
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EXAMINER PERREIRA, MELISSA JEAN				
ART UNIT 1618		PAPER NUMBER		
MAIL DATE 11/09/2010		DELIVERY MODE PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/798,876

Applicant(s)

UBER ET AL.

Examiner

MELISSA PERREIRA

Art Unit

1618

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-4, 6-139, 141 and 143-145 is/are pending in the application.
- 4a) Of the above claim(s) 42-139 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-4, 6-41, 141 and 143-145 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/15/10 has been entered.

Claims and Previous Rejections/Objections Status

2. Claims 2-4,6-139,141 and 143-145 are pending in the application. Claims 42-139 are withdrawn from consideration. Claims 1 and 140 have been canceled and claims 144 and 145 newly added in the amendment filed 10/15/10.
3. The rejection of claims 2,6-41,141 and 143-145 under 35 U.S.C. 103(a) as being unpatentable over by Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) is modified to include the references of Quay et al. (WO 96/40282), Daum et al. (US 6,231,513) and Engel (EP0135822) for simplification.

New Grounds of Rejection

4. Claims 2,6,11,13-18,20-25,27-31,36-39 and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Rossling et al. (US 6,468,506B1).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2,6,11,13-18,20-25,27-31,36-39 and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Rossling et al. (US 6,468,506B1).

7. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/plurality of differentiable populations of bubbles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles (abstract; column 1, lines 7-12; figures). The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) which may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16)** and/or liquid gas pump **(4)** (column 5, lines 5-33). The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks (column 2, lines 35-53).

8. An alternative method for the production of gaseous microparticles involves spraying the solution via a nozzle **(118)** into a column of gas where a pump **(16)** moves the solution from a tank via nozzle into a line, heat exchanger **(15)** and column of gas **(12)**, etc. (column 3, lines 22-56). The size of the resulting particles may be controlled

by the nozzle size, shape, type (not excluding those of the instant claims) as well as the working pressure and temperature in the column (column 3, lines 22-56).

9. Figure 1 shows the apparatus for the production of gaseous microparticles. It is also disclosed that a resuspended solution of gaseous microparticles may be filtered immediately before injection into a patient to increase the reliability (column 3, lines 60+; column 4, lines 13-15). The gaseous microparticles/bubble medium system of the disclosure encompasses the gaseous microparticles/bubble medium system of the instant claims and thus is capable of generating microbubbles/bubbles during a medical procedure.

10. Rossling et al. does not explicitly disclose a controller or a plurality of gases/gas-liquid interfaces.

11. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the controller may be a scientist that can manually change an operating parameter, such as composition of the bubbles in the medium, etc. and thus the system/apparatus of the disclosure does not exclude a controller.

12. Also, at the time of the invention one ordinarily skilled in the art would have a reasonable expectation of success for introducing a plurality of gases via inlets in the system/apparatus of Rossling et al. to vary/enhance the desired microbubble composition.

13. It is respectfully pointed out that instant claim 11 is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability

of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

14. Claims 2-4,6-41,141 and 143-145 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Uber, III et al. (US 6,397,098) and in further view of Quay et al. (WO 96/40282) or in further view of Daum et al. (US 6,231,513) and Engel (EP0135822).

15. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/plurality of differentiable populations of bubbles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles (abstract; column 1, lines 7-12; figures). The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) which may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16)** and/or liquid gas pump **(4)** (column 5, lines 5-33). The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks (column 2, lines 35-53) as well all that is stated above with regard to Rossling et al.

16. Rossling et al. does not disclose an imaging unit or a fluid verification device.

17. Uber, III et al. (US 6,397,098) discloses a system for producing a contrast-enhanced medical image of a patient including a source of a contrast or enhancement medium; a pressurizing unit in fluid connection with the source of contrast or enhancement medium; an imaging unit and a control unit (abstract; column 2, lines 22-45; column 5, lines 29-47). Communication between devices of the present invention is enabled through use of a control/communication interface to which each of the devices of the imaging/injection system can be connected (column 4, lines 13-24; column 5, lines 48-61). The interface can also be used to terminate an injection (i.e. verification device) (column 14, lines 9-29). The system of the disclosure includes a concentration regulator (i.e. verification device) which selectively destroys microbubbles (column 8, lines 56-65). The concentration regulator also encompasses the filter of the instant claims as it removes bubbles, not excluding those having a diameter greater than a predetermined size. The contrast or enhancement medium being gas filled microspheres containing a therapeutic agent or is also called the fluid medium, being a liquid, gas or solid suspended in a liquid or a gas. The imaging unit provides (preferably in real-time) an indication (for example, a visual or audible indication) of an internal state, condition or view of the patient based upon a signal resulting from the energy applied to the region of a patient. The pressurizing unit is in fluid connection with the source of fluid medium to pressurize the fluid medium for injection into the patient (column 3, lines 38-52).
18. Uber, III et al. also discloses the method for adjusting the condition of a fluid medium, described above, during an imaging procedure (column 4, lines 57+). The

control unit is adapted to adjust the conditions (i.e. contrast medium concentration, flow rate of the contrast medium, etc.) of the contrast or enhancement medium in the patient based upon the signal resulting from the energy applied to the region of the patient. The system may include general components or pieces of equipment, i.e. injector, etc (column 2, lines 22-53; column 3, lines 65+; column 4, lines 26-50).

19. At the time of the invention it would have been obvious to one ordinarily skilled in the art to create gaseous microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Uber, III et al. for direct administration of the contrast agent to a patient as Uber, III et al. teaches that the pressurizing unit of the system (Uber, III et al.) is in fluid connection with the source of fluid medium (contrast or enhancement medium) to pressurize the fluid medium for the advantage of direct injection into the patient. Uber, III et al. also teaches that the system may include general components or pieces of equipment manufactured by more than one company (Uber, III et al. column 2, lines 42-45), not excluding the system for generating microbubbles of Rossling et al.

20. In regards to the instant claim 19:

21. Rossling et al. does not disclose the production of microbubbles via the introduction of solid particles

22. Quay et al. (WO 96/40282) discloses the enhance production of gaseous microbubbles via the introduction of solid particles in the gas-liquid emulsion where there is a significant increase in bubble population per unit volume (abstract; p6, lines 7-

12; p8, lines 7-25). The activation process of the disclosure provides for enhancement of the contrast in an ultrasound image generated during medical diagnosis (p4, lines 4-11).

23. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via nucleation with solid particles as it is a known technique in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

24. In regards to the instant claims 26,32-35,40 and 41 :

25. Rossling et al. does not disclose the production of microbubbles via ultrasound/introduction of a plate.

26. Daum et al. (US 6,231,513) discloses a microbubble forming arrangement having a plurality of microholes which when a gas is passed through causes the gas to form numerous microbubbles in fluid (column 3, lines 1-6). The microbubble forming arrangement includes multi-perforated membrane (two dimensional material that includes microholes) or porous matrix (three dimensional structure which includes microholes) (column 3, lines 7-24). The microbubble forming arrangement may be formed from polytetrafluoroethylene, polyethylene, ceramic, sintered alloy, etc. (column 3, lines 7-23). Daum et al. also discloses the use of piezoelectric ultrasound for the preparation of gas-filled microbubbles used for ultrasound diagnosis (column 4, lines 10-24).

27. Engel (EP0135822) discloses a diffuser (plate) or a series-arrangement for the throughpassage of a fluid having a multitude of channels which extend therethrough in a mutually parallel relationship (abstract). The diffuser enables a particularly uniform distribution of the fluid over large surface areas (p1, lines 24-28) and the generation of a stream of fine bubbles (p4, lines 1-8). The permeable plate may further comprise a water-permeable layer for draining purposes (p2, lines 25-30; p4, lines 9-24).

28. At the time of the invention it would have been obvious to one ordinarily skilled in the art to generate microparticles via piezoelectric ultrasound or induction plate as they are known techniques in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus provides enhanced imaging.

29. It is respectfully pointed out that instant claim 11 is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Response to Arguments

30. Applicant's arguments filed 10/15/10 have been fully considered but they are not persuasive.

31. Applicant asserts that the invention of the instant claims "provide an apparatus that creates microbubbles on demand within a medium, which is intended for contemporaneous injection into a patient..."

32. The instant claims are drawn to a product and not the method for delivery of microbubbles. The recitation of, "created according to the demands of a medical procedure" does not impart any patentability to the instant claims as there aren't any limitations recited in regards to the medical procedure and a medical procedure can vary from a short procedure to a long procedure, such as minutes to hours, respectively. Thus, the microbubbles of the disclosures can be prepared in real time, not excluding during a medical procedure.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618